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NEWS 5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6	Mar 08	Gene Names now available in BIOSIS
NEWS 7	Mar 22	TOXLIT no longer available
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NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
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NEWS 15	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 18	Apr 22	Federal Research in Progress (FEDRIP) now available

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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FILE 'HOME' ENTERED AT 12:05:17 ON 25 APR 2002

=> file medline, uspatful, dgene, embase, frosti, fsta, biosis, jicst, japio

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=> s factor VII/vWF-complex

'VWF-COMPLEX' IS NOT A VALID FIELD CODE
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'VWF-COMPLEX' IS NOT A VALID FIELD CODE
L1             0 FACTOR VII/VWF-COMPLEX

=> s factor VIII

   7 FILES SEARCHED...
L2         45210 FACTOR VIII

=> s vWF

L3         11612 VWF

=> s l2 and l3

L4          2771 L2 AND L3

=> s cation-exchanger
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L5 4273 CATION-EXCHANGER

=> s vWF multimer

L6 219 VWF MULTIMER

=> s l5 and l4

L7 0 L5 AND L4

=> s l4 and preparation

L8 337 L4 AND PREPARATION

=> s l4 and recovery

L9 179 L4 AND RECOVERY

=> s l9 and l5

L10 0 L9 AND L5

=> s l9 and l6

L11 7 L9 AND L6

=> d l11 ti abs ibib tot

L11 ANSWER 1 OF 7 MEDLINE
TI Effects of human recombinant, plasma-derived and porcine von Willebrand factor in pigs with severe von Willebrand disease.
AB The effects of the infusion of a human recombinant von Willebrand factor (**vWF**) preparation in pigs homozygous for von Willebrand disease (vWD) were evaluated on serial measurements of von Willebrand factor antigen and activity, FVIII activity, **vWF multimer** analysis, in-vivo bleeding time and platelet adhesion and thrombus formation on collagen at high shear rates in an ex-vivo model of experimental thrombosis. Plasma-derived human and porcine **vWF** were used for comparison. Before infusion, the pigs were characterized by undetectable plasma **vWF** levels, a low level of FVIII, prolonged bleeding time, severely impaired platelet adhesion and thrombus formation.
After infusion of the human recombinant **vWF**, in-vivo **recovery** of **vWF** activity ranged from 58% to 82%, depending on the dose infused, and its half-life was longer than for the plasma-derived concentrates. The highest-molecular-weight forms of human recombinant **vWF** were removed from the circulation gradually. Infusion of the three **vWF** concentrates produced inconsistent effects on bleeding time and moderate improvement of platelet adhesion and thrombus formation. After infusion, a prolonged increase of FVIII (> 48 h) was observed, suggesting that human recombinant **vWF** is able to bind and to stabilize porcine **factor VIII** and that porcine vWD is a good model for studying such interactions.
ACCESSION NUMBER: 1998353118 MEDLINE
DOCUMENT NUMBER: 98353118 PubMed ID: 9690808
TITLE: Effects of human recombinant, plasma-derived and porcine von Willebrand factor in pigs with severe von Willebrand disease.
AUTHOR: Roussi J; Turecek P L; Andre P; Bonneau M; Pignaud G; Bal

dit Sollier C; Schlokat U; Dorner F; Schwarz H P; Drouet L
CORPORATE SOURCE: INSERM U 353, Hopital Saint Louis, Paris, France..
ja[redacted]eline.roussi@rpc.ap-hop-paris.f[redacted]
SOURCE: BLOOD COAGULATION AND FIBRINOLYSIS, (1998 Jun) 9 (4) 361-72.
Journal code: A5J; 9102551. ISSN: 0957-5235.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 19990129
Entered Medline: 19981021

L11 ANSWER 2 OF 7 MEDLINE
TI Abnormal VIII: von Willebrand factor patterns in the plasma of patients with the hemolytic-uremic syndrome.
AB Plasma VIII:von Willebrand factor antigen (VIII:**vWF**) levels were elevated approximately two- to eightfold in seven patients (three adults and four children) during acute episodes of thrombocytopenia, renal failure, and hemolytic anemia (the hemolytic-uremic syndrome, HUS). In all seven patients, there was an alteration in plasma VIII:**vWF** patterns during these acute HUS episodes, so that the largest VIII: **vWF** forms were relatively decreased. Plasma VIII:**vWF** **multimer** patterns returned to normal, or nearly to normal, as platelet counts returned to preexisting levels, even in the patients whose **recovery** of renal function was incomplete and whose plasma VIII: **vWF** antigen level remained above normal. The sister of one of the HUS patients had a similar clinical prodrome (gastroenteritis) that was not followed by thrombocytopenia or renal failure and was not accompanied by an elevated level or abnormal forms of plasma VIII:**vWF**. These results suggest that an alteration in VIII:**vWF** metabolism, distribution, or interaction with platelets is associated with acute HUS episodes. In contrast to patients with chronic relapsing thrombotic thrombocytopenic purpura, none of the HUS patients (either during or after the acute HUS episodes) had a defect in the conversion of unusually large VIII:**vWF** multimers derived from endothelial cells to the VIII: **vWF** forms found in normal plasma.
ACCESSION NUMBER: 84281374 MEDLINE
DOCUMENT NUMBER: 84281374 PubMed ID: 6432074
TITLE: Abnormal VIII: von Willebrand factor patterns in the plasma of patients with the hemolytic-uremic syndrome.
AUTHOR: Moake J L; Byrnes J J; Troll J H; Rudy C K; Weinstein M J; Colannino N M; Hong S L
CONTRACT NUMBER: HL13262 (NHLBI)
HL22355 (NHLBI)
SOURCE: BLOOD, (1984 Sep) 64 (3) 592-8.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198409
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19840926

L11 ANSWER 3 OF 7 USPATFULL
TI Stable **factor VIII** / **vWF**-complex

AB There are disclosed a stable **factor VIII/vWF** -complex, particularly comprising high-molecular **vWF** multimers, being free from low-molecular **vWF** molecules and from proteolytic **vWF** degradation products, as well as a method of producing this complex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2002:43190 USPATFULL		
TITLE:	Stable **factor VIII / vWF** -complex		
INVENTOR(S):	Fischer, Bernhard, Vienna, AUSTRIA Mitterer, Artur, Mannsdorf, AUSTRIA Dorner, Friedrich, Vienna, AUSTRIA Eibl, Johann, Vienna, AUSTRIA		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002025556	A1	20020228
APPLICATION INFO.:	US 2001-849484	A1	20010507 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1998-142768, filed on 6 Nov 1998, GRANTED, Pat. No. US 6228613 A 371 of International Ser. No. WO 1997-AT55, filed on 13 Mar 1997, UNKNOWN		
	NUMBER	DATE	
PRIORITY INFORMATION:	AT 1996-494	19960315	
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	HELLER EHRMAN WHITE & MCAULIFFE LLP, 1666 K STREET,NW, SUITE 300, WASHINGTON, DC, 20006		
NUMBER OF CLAIMS:	43		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	9 Drawing Page(s)		
LINE COUNT:	1141		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 4 OF 7 USPATFULL

TI Stable **factor VIII**/von Willebrand factor complex

AB There are disclosed a stable **factor VIII/vWF** -complex, particularly comprising high-molecular **vWF** multimers, being free from low-molecular **vWF** molecules and from proteolytic **vWF** degradation products, as well as a method of producing this complex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2001:67424 USPATFULL		
TITLE:	Stable **factor VIII**/von Willebrand factor complex		
INVENTOR(S):	Fischer, Bernhard, Vienna, Austria Mitterer, Artur, Mannsdorf, Austria Dorner, Friedrich, Vienna, Austria Eibl, Johann, Vienna, Austria		
PATENT ASSIGNEE(S):	Baxter Aktiengesellschaft, Vienna, Austria (non-U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6228613	B1	20010508
	WO 9734930		19970925
APPLICATION INFO.:	US 1998-142768		19981106 (9)
	WO 1997-AT55		19970313
			19981106 PCT 371 date
			19981106 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	AT 1996-494	19960315
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Carlson, Karen Cochrane	
ASSISTANT EXAMINER:	Robinson, Hope A.	
LEGAL REPRESENTATIVE:	Heller Ehrman White & McAuliffe	
NUMBER OF CLAIMS:	40	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 9 Drawing Page(s)	
LINE COUNT:	1098	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 5 OF 7 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

TI Effects of human recombinant, plasma-derived and porcine von Willebrand factor in pigs with severe von Willebrand disease.

AB The effects of the infusion of a human recombinant von Willebrand factor (**vWF**) preparation in pigs homozygous for von Willebrand disease (vWD) were evaluated on serial measurements of von Willebrand factor antigen and activity, FVIII activity, **vWF multimer** analysis, in-vivo bleeding time and platelet adhesion and thrombus formation on collagen at high shear rates in an ex-vivo model of experimental thrombosis. Plasma-derived human and porcine **vWF** were used for comparison. Before infusion, the pigs were characterized by undetectable plasma **vWF** levels, a low level of FVIII, prolonged bleeding time, severely impaired platelet adhesion and thrombus formation.

After infusion of the human recombinant **vWF**, in-vivo **recovery** of **vWF** activity ranged from 58% to 82%, depending on the dose infused, and its half-life was longer than for the plasma-derived concentrates. The highest-molecular- weight forms of human recombinant **vWF** were removed from the circulation gradually. Infusion of the three **vWF** concentrates produced inconsistent effects on bleeding time and moderate improvement of platelet adhesion and thrombus formation. After infusion, a prolonged increase of FVIII (> 48 h) was observed, suggesting that human recombinant **vWF** is able to bind and to stabilize porcine **factor VIII** and that porcine vWD is a good model for studying such interactions.

ACCESSION NUMBER:	1998214481 EMBASE
TITLE:	Effects of human recombinant, plasma-derived and porcine von Willebrand factor in pigs with severe von Willebrand disease.
AUTHOR:	Roussi J.; Turecek P.L.; Andre P.; Bonneau M.; Pignaud G.; Dit Sollier C.B.; Schlokat U.; Dorner F.; Schwarz H.-P.; Drouet L.
CORPORATE SOURCE:	Dr. J. Roussi, Laboratoire d'Hematologie, Hopital Raymond Poincare, 104 Boulevard Raymond Poincare, 92380 Garches, France. jacqueline.roussi@rpc.ap-hop-paris.fr
SOURCE:	Blood Coagulation and Fibrinolysis, (1998) 9/4 (361-372). Refs: 42 ISSN: 0957-5235 CODEN: BLFIE7
COUNTRY:	United Kingdom
DOCUMENT TYPE:	Journal; Article
FILE SEGMENT:	018 Cardiovascular Diseases and Cardiovascular Surgery 025 Hematology
LANGUAGE:	English
SUMMARY LANGUAGE:	English

L11 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI Effects of human recombinant, plasma-derived and porcine von Willebrand factor in pigs with severe von Willebrand disease.

AB The effects of the infusion of a human recombinant Willebrand factor (**vWF**) preparation in pigs homozygous for von Willebrand disease (vWD) were evaluated on serial measurements of von Willebrand factor antigen and activity, FVIII activity, **vWF multimer** analysis, in-vivo bleeding time and platelet adhesion and thrombus formation on collagen at high shear rates in an ex-vivo model of experimental thrombosis. Plasma-derived human and porcine **vWF** were used for comparison. Before infusion, the pigs were characterized by undetectable plasma **vWF** levels, a low level of FVIII, prolonged bleeding time, severely impaired platelet adhesion and thrombus formation.

After infusion of the human recombinant **vWF**, in-vivo **recovery** of **vWF** activity ranged from 58% to 82%, depending on the dose infused, and its half-life was longer than for the plasma-derived concentrates. The highest-molecular-weight forms of human recombinant **vWF** were removed from the circulation gradually. Infusion of the three **vWF** concentrates produced inconsistent effects on bleeding time and moderate improvement of platelet adhesion and thrombus formation. After infusion, a prolonged increase of FVIII (> 48 h) was observed, suggesting that human recombinant **vWF** is able to bind and to stabilize porcine **factor VIII** and that porcine vWD is a good model for studying such interactions.

ACCESSION NUMBER: 1998:342972 BIOSIS
DOCUMENT NUMBER: PREV199800342972
TITLE: Effects of human recombinant, plasma-derived and porcine von Willebrand factor in pigs with severe von Willebrand disease.
AUTHOR(S): Roussi, J. (1); Turecek, P. L.; Andre, P.; Bonneau, M.; Pignaud, G.; Bal Dit Sollier, C.; Schlokat, U.; Dorner, F.; Schwarz, H.-P.; Drouet, L.
CORPORATE SOURCE: (1) Laboratoire d'Hematologie, Hopital Raymond Poincare, 104 Boulevard Raymond Poincare, 92380 Garches France
SOURCE: Blood Coagulation & Fibrinolysis, (June, 1998) Vol. 9, No. 4, pp. 361-372.
ISSN: 0957-5235.
DOCUMENT TYPE: Article
LANGUAGE: English

L11 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

TI ABNORMAL **FACTOR-VIII** VON WILLEBRAND FACTOR PATTERNS IN THE PLASMA OF PATIENTS WITH THE HEMOLYTIC-UREMIC SYNDROME.

AB Plasma VIII:von Willebrand factor antigen (VIII:**vWF**) levels were elevated .apprx. 2- to 8-fold in 7 patients (3 adults and 4 children) during acute episodes of thrombocytopenia, renal failure and hemolytic anemia (the hemolytic-uremic syndrome, HUS). In all 7 patients, there was an alteration in plasma VIII:**vWF** patterns during these acute HUS episodes, so that the largest VIII:**vWF** forms were relatively decreased. Plasma VIII:**vWF multimer** patterns returned to normal, or nearly to normal, as platelet counts returned to preexisting levels, even in the patients whose **recovery** of renal function was incomplete and whose plasma VIII:**vWF** antigen level remained above normal. The sister of 1 of the HUS patients had a similar clinical prodrome (gastroenteritis) that was not followed by thrombocytopenia or renal failure and was not accompanied by an elevated level or abnormal forms of plasma VIII:**vWF**. An alteration in VIII:**vWF** metabolism, distribution or interaction with platelets apparently is associated with acute HUS episodes. In contrast to patients with chronic

relapsing thrombotic thrombocytopenic purpura, none of the HUS patients (either during or after the acute HUS episodes) had a defect in the conversion of unusually large VIII:**vWF** multimers derived from endothelial cells to the VIII:**vWF** forms found in normal plasma.

ACCESSION NUMBER: 1985:220836 BIOSIS
DOCUMENT NUMBER: BA79:832
TITLE: ABNORMAL **FACTOR-VIII** VON WILLEBRAND FACTOR PATTERNS IN THE PLASMA OF PATIENTS WITH THE HEMOLYTIC-UREMIC SYNDROME.
AUTHOR(S): MOAKE J L; BYRNES J J; TROLL J H; RUDY C K; WEINSTEIN M J; COLANNINO N M; HONG S L
CORPORATE SOURCE: MED. HEMATOL. SECT. METHODIST HOSP.., 6565 FANNIN, MAIL STN. 902-MAIN BUILD., HOUSTON, TEX. 77030.
SOURCE: BLOOD, (1984) 64 (3), 592-598.
CODEN: BLOOAW. ISSN: 0006-4971.
FILE SEGMENT: BA; OLD
LANGUAGE: English

=> d his

(FILE 'HOME' ENTERED AT 12:05:17 ON 25 APR 2002)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, FROSTI, FSTA, BIOSIS, JICST-EPLUS, JAPIO' ENTERED AT 12:07:17 ON 25 APR 2002

L1 0 S FACTOR VII/VWF-COMPLEX
L2 45210 S FACTOR VIII
L3 11612 S VWF
L4 2771 S L2 AND L3
L5 4273 S CATION-EXCHANGER
L6 219 S VWF MULTIMER
L7 0 S L5 AND L4
L8 337 S L4 AND PREPARATION
L9 179 S L4 AND RECOVERY
L10 0 S L9 AND L5
L11 7 S L9 AND L6

=> d l9 ti abs ibib 1-10

L9 ANSWER 1 OF 179 MEDLINE
TI What's happening? The quality of methylene blue treated FFP and cryo.
AB It is currently unclear to what degree methylene blue in combination with removal, of cells from plasma, by filter, can directly influence the loss of active components of plasma and whether the co-precipitation of FVIII/**vWf** with fibrinogen/fibronectin is affected by combined methylene blue and light treatment (MBLT). These questions are investigated using the Fenwal system. Our results indicate that up to 15% of the FVIII and IX
are lost due to exposure of plasma to filters and methylene blue (MB). The
illumination leads to a further 10-15% loss of all other major clotting factors. Factor XI appears to be highly sensitive to the MBLT-process, while inhibitors of the coagulation system are less affected. MBLT did not
grossly influence the distribution of fVIII/**vWf**:Ag between cryoprecipitate and cryosupernatant using a paired control/test protocol, although the fVIII/**vWf recovery** is reduced in MBLT samples. The three commercially available MBLT processes differ in terms of operational aspects. These may have some impact on overall quality/safety and bioequivalency.
ACCESSION NUMBER: 2002113858 MEDLINE
DOCUMENT NUMBER: 21834712 PubMed ID: 11846153

TITLE: What's happening? The quality of methylene blue treated FFP
an[redacted]ryo.
AUTHOR: Seghatchian J; Krailadsiri P
CORPORATE SOURCE: National Blood Service, London, England, UK..
jseghatchian@hotmail.com
SOURCE: Transfus Apheresis Sci, (2001 Dec) 25 (3) 227-31.
Journal code: 101095653. ISSN: 1473-0502.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: T
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020216
Last Updated on STN: 20020320
Entered Medline: 20020319

L9 ANSWER 2 OF 179 MEDLINE
TI Pharmacokinetic studies with FVIII/von Willebrand factor concentrate can be a diagnostic tool to distinguish between subgroups of patients with acquired von Willebrand syndrome.
AB Acquired von Willebrand syndrome (AVWS) has been associated mainly with monoclonal gammopathy of uncertain significance (MGUS), clonal lymphoproliferative or myeloproliferative disorders and autoimmunity. In the present work we studied 6 patients with AVWS: four with MGUS IgG (lambda or kappa), one with small lymphocytic lymphoma and one with agnogenic myeloid metaplasia (AMM). All the patients underwent a pharmacokinetic analysis at presentation in order to study potential differences in **recovery**, clearance (CL) or terminal half-life (THL) following administration of von Willebrand factor (**VWF**) concentrate. In all the patients with AVWS an increase in clearance and a decrease in THL was observed as compared to these parameters in patients with hereditary type 3 von Willebrand disease (VWD). No difference in **recovery** was observed among the groups. The increase in clearance and the decrease in THL were significantly more pronounced in the group of
MGUS patients (57.93 +/- 25.6 ml/h/kg, and 1.39 +/- 0.5 h, respectively) as compared to these parameters in the AMM (8.06 ml/h/kg, and 6.96 h, respectively) or the lymphoma (4.76 ml/h/kg, and 6.76 h. respectively) patients (p = 0.03 for clearance and 0.001 for THL). These data indicate that the pharmacokinetic analysis can be a useful tool to distinguish between MGUS-related and other causes of AVWS, and to plan an appropriate treatment accordingly.
ACCESSION NUMBER: 2002010416 MEDLINE
DOCUMENT NUMBER: 21265562 PubMed ID: 11372672
TITLE: Pharmacokinetic studies with FVIII/von Willebrand factor concentrate can be a diagnostic tool to distinguish between
subgroups of patients with acquired von Willebrand syndrome.
AUTHOR: Luboshitz J; Lubetsky A; Schliamser L; Kotler A; Tamarin I;
Inbal A
CORPORATE SOURCE: Institute of Thrombosis and Hemostasis, Sheba Medical Center, Tel Hashomer, Tel-Aviv University, Israel.
SOURCE: THROMBOSIS AND HAEMOSTASIS, (2001 May) 85 (5) 806-9.
Journal code: 7608063. ISSN: 0340-6245.
PUB. COUNTRY: Germany: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020220

Entered Medline: 20020219

L9 ANSWER 3 OF 179 MEDLINE
TI Coagulation factor content of cryoprecipitate prepared from methylene blue
plus light virus-inactivated plasma.
AB Levels of **factor VIII** (FVIII) and fibrinogen were
assessed in control cryoprecipitate and cryoprecipitate prepared in two centres from plasma subjected to methylene blue (MB) photochemical virus inactivation. The level of coagulation FVIII activity was reduced in plasma by approximately 30% after MB photoinactivation, with only 44% (centre A) and 31% (centre B) of units meeting the current UK specification of 0.7 iu/ml. A revised specification of 0.5 iu/ml is suggested. Losses of less than 11% were seen for von Willebrand factor (**VWF**)-related activities. Cryoprecipitate prepared from group O or group A MB-treated plasma contained 27-40% less FVIII than control units. This reflected the lower levels in MB-treated plasma. The concentrating power of the cryoprecipitation process was not reduced for FVIII or fibrinogen in MB-treated units. MB cryoprecipitate from centre A still met
the UK guideline specification for FVIII and fibrinogen content, whereas at centre B only 62.5% of the group O cryoprecipitates contained > 70 iu FVIII/unit. This may reflect the lower product volume and lower FVIII content of group O plasma used at centre B and suggests that maintenance of total coagulation factor **recovery** in MB-treated cryoprecipitate will require the higher product volume.
ACCESSION NUMBER: 2000345427 MEDLINE
DOCUMENT NUMBER: 20345427 PubMed ID: 10886222
TITLE: Coagulation factor content of cryoprecipitate prepared from
methylene blue plus light virus-inactivated plasma.
COMMENT: Comment in: Br J Haematol. 2000 Dec;111(3):986-7
AUTHOR: Hornsey V S; Krailadsiri P; MacDonald S; Seghatchian J; Williamson L M; Prowse C V
CORPORATE SOURCE: Scottish National Blood Transfusion Service, National Science Laboratory, Edinburgh, UK..
valerie.hornsey@snbts.csa.scot.nhs.uk
SOURCE: BRITISH JOURNAL OF HAEMATOLOGY, (2000 Jun) 109 (3) 665-70.
Journal code: AXC; 0372544. ISSN: 0007-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000811
Last Updated on STN: 20010709
Entered Medline: 20000802

L9 ANSWER 4 OF 179 MEDLINE
TI Aging, physical conditioning, and exercise-induced changes in hemostatic factors and reaction products.
AB The influence of age on training-induced changes in resting and stimulated
hemostatic potential was studied in three age categories (Cat I-III; 20-30
yr, 35-45 yr, and 50-60 yr, respectively) of sedentary men before and after 12 wk of training. Coagulation, fibrinolytic activity, and activation markers (reflecting fibrin formation and degradation) were determined. Physical conditioning resulted in a more pronounced increase in von Willebrand factor (**vWF**) and **factor VIII**
clotting activity (FVIII:c) in Cat I and II and a more pronounced shortening of the activated partial thromboplastin time in all categories at maximal exertion and during **recovery**. Enhanced increases in tissue-type plasminogen activator (t-PA) antigen and activity and

single-chain (sc) urokinase-type plasminogen activator (u-PA) at maximal exercise and 5 min of **recovery** were observed in all age groups after training. The effects on FVIII:c, **vWF**, and sc[redacted]A were most pronounced in the youngest age group (Cat I). Increases in the marker of thrombin generation were highest in Cat III; no effect was seen on thrombin-antithrombin complex, plasmin-antiplasmin complex, and D-dimer in any of the age groups. We concluded that training enhances both coagulation and fibrinolytic potential during strenuous exercise. The effect on FVIII/**vWF** and t-PA/u-PA is most pronounced in younger individuals, whereas thrombin formation is most pronounced in older individuals.

ACCESSION NUMBER: 2000259491 MEDLINE
DOCUMENT NUMBER: 20259491 PubMed ID: 10797112
TITLE: Aging, physical conditioning, and exercise-induced changes in hemostatic factors and reaction products.
AUTHOR: van den Burg P J; Hospers J E; Mosterd W L; Bouma B N; Huisveld I A
CORPORATE SOURCE: Department of Medical Physiology and Sports Medicine, University of Utrecht, 3508 TA Utrecht, The Netherlands.
SOURCE: JOURNAL OF APPLIED PHYSIOLOGY, (2000 May) 88 (5) 1558-64.

Journal code: HEG; 8502536. ISSN: 8750-7587.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000706
Last Updated on STN: 20000706
Entered Medline: 20000623

L9 ANSWER 5 OF 179 MEDLINE
TI Post-trauma coagulation and fibrinolysis in children suffering from severe cerebro-cranial trauma.
AB The present study was designed to evaluate the post-trauma haemostatic changes in 27 children with severe cranio-cerebral trauma defined by a modified Glasgow Coma Score (GCS) < 10. Blood samples for coagulation studies (fibrinogen, von Willebrand factor (**vWf**), **factor VIII**:C, antithrombin, protein C, plasminogen, tissue-type plasminogen activator (t-PA), plasminogen activator inhibitor-1 (PAI), D-dimer) were obtained within two hours of admission, 24 h later, and on days 3-5, 7-9, 21 and 35. Data of this study indicate that alterations of coagulation in paediatric patients are similar to those in adults: On hospitalisation, activated haemostasis was found with decreased fibrinogen, antithrombin and protein C along with enhanced t-PA and PAI. Twenty-four hours later, hypercoagulability with significantly increased **vWF** and fibrinogen started, with a peak level within the second week. Within 24 h of admission, 17 children developed disseminated intravascular coagulation (DIC) with a clear-cut decrease of antithrombin and fibrinogen together with platelet consumption and enhanced D-dimer. The outcome of children with DIC was significantly poorer than in those without DIC. Complete **recovery** was seen in five patients; sequelae no handicap and moderate disability were each found in six patients. Severe disability was diagnosed in two children, and fulminant DIC with lethal outcome occurred in eight patients. The GCS ($P < 0.01$) and the occurrence of DIC ($P < 0.005$) showed the strongest association with the patients' clinical outcome. CONCLUSION: Our data underline the significance of post-trauma disturbances of the haemostatic system for the clinical course and outcome in children with severe cranio-cerebral

injuries.
ACCESSION NUMBER: 2000114291 MEDLINE
DOCUMENT NUMBER: 20[redacted]291 PubMed ID: 10650869
TITLE: Post-trauma coagulation and fibrinolysis in children suffering from severe cerebro-cranial trauma.
AUTHOR: Becker S; Schneider W; Kreuz W; Jacobi G; Scharrer I; Nowak-Gottl U
CORPORATE SOURCE: Department of Paediatrics, University Hospital Frankfurt am Main, Germany.. sbecker@uni-frankfurt.de
SOURCE: EUROPEAN JOURNAL OF PEDIATRICS, (1999 Dec) 158 Suppl 3 S197-202.
Journal code: END; 7603873. ISSN: 0340-6199.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000218
Last Updated on STN: 20000218
Entered Medline: 20000208

L9 ANSWER 6 OF 179 MEDLINE
TI Preclinical evaluation of recombinant von Willebrand factor in a canine model of von Willebrand disease.
AB Dutch Kooiker dogs with hereditary von Willebrand disease (vWD) have undetectable levels of von Willebrand factor (**vWF**), resulting in spontaneous hemorrhage of mucosal surfaces similar to the clinical picture of vWD in humans. We used this canine model of vWD to study the in vivo effects of a new recombinant von Willebrand factor (rvWF) preparation that contained all species of **vWF** multimers compared with an rvWF fraction containing only low molecular weight multimers (LMW-rvWF) and with a plasma-derived **factor VIII/vWF** concentrate (pdvWF). Administration of rvWF in these **vWF** -deficient dogs resulted in a **vWF**:Ag half-life of 21.6 hours in one dog and 22.1 hours in a second dog. Administration of pdvWF resulted in a half-life for **vWF**:Ag of 7.7 hours, and LMW-rvWF, 9 hours. The in vivo **recovery** of **vWF**:Ag after administration of rvWF was 59, 64 and 70% in three dogs, respectively; 33% after pdvWF, and 92% after LMW-rvWF. The in vivo **recovery** of ristocetin cofactor (RCoF) was 78, 110 and 120% for rvWF, and 25% for pdvWF. Both rvWF and pdvWF caused increases in **factor VIII**. Although no effect was seen on bleeding time at the dosages used, the rate of blood flow from cuticle wounds was reduced after a single bolus administration of rvWF. The rvWF was able to control a severe nose bleed in one dog.
ACCESSION NUMBER: 1999242935 MEDLINE
DOCUMENT NUMBER: 99242935 PubMed ID: 10226348
TITLE: Preclinical evaluation of recombinant von Willebrand factor in a canine model of von Willebrand disease.
AUTHOR: Schwarz H P; Dorner F; Mitterer A; Mundt W; Schlokat U; Pichler L; Turecek P L
CORPORATE SOURCE: Baxter Hyland Immuno, Vienna, Austria.. schwarh@baxter.com
SOURCE: WIENER KLINISCHE WOCHENSCHRIFT, (1999 Mar 12) 111 (5) 181-91.
Journal code: XOP; 21620870R. ISSN: 0043-5325.
PUB. COUNTRY: Austria
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990715

Last Updated on STN: 19990715
Entered Medline: 19990702

L9 ANSWER 7 OF 179 MEDLINE

TI Intranasal DDAVP induced increases in plasma von Willebrand factor alter the pharmacokinetics of high-purity **factor VIII** concentrates in severe haemophilia A patients.

AB Because native circulating **factor VIII** (FVIII) is maximally stabilized when it is bound to von Willebrand factor (**vWf**), increased plasma **vWf** levels may enhance the infused FVIII concentrate intravascular survival and efficacy in severe haemophiliacs. To assess whether the kinetic characteristics and **recovery** of high purity, plasma-derived (Monoclate-P, Centeon) and recombinant (Bioclate , Centeon) FVIII concentrates are enhanced by increased plasma **vWf** concentrations, we compared the pharmacokinetic response to a bolus of FVIII infused alone with the response to a bolus infused 2 h after the intranasal delivery of 300 microg of desmopressin acetate (DDAVP) High Concentration Nasal Spray (Stimate, Centeon) in 10 adult severe haemophiliacs. FVIII activity was determined using a one-stage clotting assay on cryopreserved plasma specimens obtained at baseline and at 14 distinct time points (0.25-48 h) following the FVIII infusions. Ristocetin co-factor activity (RCoFA) and **vWf** antigen levels were assayed at baseline and 2 h after Stimate. FVIII kinetic parameters were calculated using standard, noncompartmental kinetic methods. Statistical analysis was performed using a paired t-test with 95% confidence limits. The mean rises in RCoFA (0.65+/-0.44 IU mL(-1)) and **vWf** antigen (0.19+/-0.07 IU mL-1) induced by Stimate were significant (P<0.01 and P<0.0001, respectively). The mean increases in the volume of distribution at steady state (Vss) (13.2+/-9.3 dL) and mean residence time (MRT) (4.4+/-3.9 h) between the FVIII-only arm and the FVIII plus Stimate arm were highly significant (P = 0.0015 and P = 0.0059, respectively). The mean differences in **recovery**, area under the curve (AUC), half-life, and clearance (Cl) were not significantly altered. Subgroup analysis revealed statistically significant increases in Vss and MRT (P = 0.025 and P = 0.012, respectively) following the administration of intranasal DDAVP in the Monoclate-P cohort, but not in the Bioclate group. These data suggest that even modest pharmacologically induced increases in plasma **vWf** can favourably affect the kinetics of high-purity, plasma-derived FVIII concentrates in severe haemophiliacs.

ACCESSION NUMBER: 1999234408 MEDLINE
DOCUMENT NUMBER: 99234408 PubMed ID: 10215955
TITLE: Intranasal DDAVP induced increases in plasma von Willebrand factor alter the pharmacokinetics of high-purity **factor VIII** concentrates in severe haemophilia A patients.
AUTHOR: Deitcher S R; Tuller J; Johnson J A
CORPORATE SOURCE: The University of Tennessee Comprehensive Hemophilia Center, Department of Medicine, The University of Tennessee, Memphis, USA.
CONTRACT NUMBER: RR00211 (NCRR)
SOURCE: HAEMOPHILIA, (1999 Mar) 5 (2) 88-95.
Journal code: C8F; 9442916. ISSN: 1351-8216.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990715
Last Updated on STN: 19990715
Entered Medline: 19990707

L9 ANSWER 8 OF 179 MEDLINE
TI Evaluation of recombinant von Willebrand factor in a canine model of von Willebrand disease.
AB Dutch Kooiker dogs with hereditary von Willebrand disease have undetectable levels of von Willebrand factor (**vWF**), resulting in spontaneous haemorrhage of mucosal surfaces similar to the clinical picture of von Willebrand disease in humans. We used this canine model of von Willebrand disease to study the in vivo effects of a new recombinant von Willebrand factor (rvWF) preparation that contained all species of **vWF** multimers compared with a rvWF fraction containing only low molecular weight multimers (LMW-rvWF) and with a plasma-derived **factor VIII/vWF** concentrate (pdvWF).
Administration of rvWF in these **vWF**-deficient dogs resulted in a **vWF**:Ag half-life of 21.6 h in one dog and 22.1 h in a second dog. Administration of pdvWF resulted in a half-life for **vWF**:Ag of 7.7 h, and LMW-rvWF, 9 h. The in vivo **recovery** of **vWF**:Ag after administration of rvWF was 59%, 64% and 70% in three dogs, respectively; 33% after pdvWF, and 92% after LMW-rvWF. The in vivo **recovery** of ristocetin cofactor (RCoF) was 78%, 110% and 120% for rvWF, and 25% for pdvWF. Both rvWF and pdvWF caused increases in FVIII. Although no effect was seen on bleeding time at the dosages used, the rate of blood flow from cuticle wounds was reduced after a single bolus administration of rvWF. The rvWF was able to control a severe nose bleed in one dog.
ACCESSION NUMBER: 1999152674 MEDLINE
DOCUMENT NUMBER: 99152674 PubMed ID: 10028320
TITLE: Evaluation of recombinant von Willebrand factor in a canine model of von Willebrand disease.
AUTHOR: Schwarz H P; Dorner F; Mitterer A; Mundt W; Schlokat U; Pichler L; Turecek P L
CORPORATE SOURCE: Hyland Immuno Division, Baxter Healthcare, Vienna, Austria.. schwarh@baxter.com
SOURCE: HAEMOPHILIA, (1998) 4 Suppl 3 53-62.
Journal code: C8F; 9442916. ISSN: 1351-8216.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990324
Last Updated on STN: 19990324
Entered Medline: 19990311

L9 ANSWER 9 OF 179 MEDLINE
TI Pharmacokinetics, efficacy and safety of Humate-P in von Willebrand disease.
AB In a pharmacokinetic study with Humate-P including six patients with various types of von Willebrand disease, a median half-life of 11.3 h for **vWF**:RCoF and of 15.2 h for **vWF**:Ag was found. The median value of in vivo **recovery** (IVR) was estimated for **vWF**:RCoF as 2.10 IU dL-1 plasma per 1 substituted IU kg-1 b.w. (or 73%), for **vWF**:Ag as 1.88 IU dL-1 plasma per 1 substituted IU kg-1 b.w. (or 69%); and for FVIII:C as 2.69 IU dL-1 plasma per 1 IU kg-1 b.w. (or 99%). Transient postinfusion shortening or normalization of previously prolonged bleeding time was observed in all patients. In a retrospective study involving 97 patients with various von Willebrand disease types, clinical efficacy and safety of treatment with Haemate-P in 73 surgical interventions, 344 separate bleeding events, 93 other events and 20 cycles of prophylactic treatment were evaluated. The clinical efficacy was rated

good to excellent in 99% of the surgeries, in 97% of the bleeding episodes, in 86% of the other events, and in all prophylactic treatments. The overall tolerability was good. Adverse events possibly or probably associated with use of Humate-P/Haemate-P were rare, of non-serious nature
and mild to moderate in their intensity.

ACCESSION NUMBER: 1999152670 MEDLINE
DOCUMENT NUMBER: 99152670 PubMed ID: 10028316
TITLE: Pharmacokinetics, efficacy and safety of Humate-P in von Willebrand disease.
AUTHOR: Dobrkovska A; Krzensk U; Chediak J R
CORPORATE SOURCE: Clinical Research & Development, Centeon Pharma GmbH, Marburg, Germany.
SOURCE: HAEMOPHILIA, (1998) 4 Suppl 3 33-9.
Journal code: C8F; 9442916. ISSN: 1351-8216.
PUB. COUNTRY: ENGLAND: United Kingdom
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990324
Last Updated on STN: 19990324
Entered Medline: 19990311

L9 ANSWER 10 OF 179 MEDLINE
TI Effects of human recombinant, plasma-derived and porcine von Willebrand factor in pigs with severe von Willebrand disease.
AB The effects of the infusion of a human recombinant von Willebrand factor (
vWF) preparation in pigs homozygous for von Willebrand disease (vWD) were evaluated on serial measurements of von Willebrand factor antigen and activity, FVIII activity, **vWF** multimer analysis, in-vivo bleeding time and platelet adhesion and thrombus formation on collagen at high shear rates in an ex-vivo model of experimental thrombosis. Plasma-derived human and porcine **vWF** were used for comparison. Before infusion, the pigs were characterized by undetectable plasma **vWF** levels, a low level of FVIII, prolonged bleeding time, severely impaired platelet adhesion and thrombus formation. After infusion of the human recombinant **vWF**, in-vivo **recovery** of **vWF** activity ranged from 58% to 82%, depending on the dose infused, and its half-life was longer than for the plasma-derived concentrates. The highest-molecular-weight forms of human recombinant **vWF** were removed from the circulation gradually. Infusion of the three **vWF** concentrates produced inconsistent effects on bleeding time and moderate improvement of platelet adhesion and thrombus formation.
After infusion, a prolonged increase of FVIII (> 48 h) was observed, suggesting that human recombinant **vWF** is able to bind and to stabilize porcine **factor VIII** and that porcine vWD is a good model for studying such interactions.

ACCESSION NUMBER: 1998353118 MEDLINE
DOCUMENT NUMBER: 98353118 PubMed ID: 9690808
TITLE: Effects of human recombinant, plasma-derived and porcine von Willebrand factor in pigs with severe von Willebrand disease.
AUTHOR: Roussi J; Turecek P L; Andre P; Bonneau M; Pignaud G; Bal dit Sollier C; Schlokat U; Dorner F; Schwarz H P; Drouet L
CORPORATE SOURCE: INSERM U 353, Hopital Saint Louis, Paris, France.. jacqueline.roussi@rpc.ap-hop-paris.fr
SOURCE: BLOOD COAGULATION AND FIBRINOLYSIS, (1998 Jun) 9 (4) 361-72.
Journal code: A5J; 9102551. ISSN: 0957-5235.
PUB. COUNTRY: ENGLAND: United Kingdom

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                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199810
ENTRY DATE:         Entered STN: 19981029
                    Last Updated on STN: 19990129
                    Entered Medline: 19981021


=> s high or low multimer

   2 FILES SEARCHED...
L12    7046491 HIGH OR LOW MULTIMER

=> d his


     (FILE 'HOME' ENTERED AT 12:05:17 ON 25 APR 2002)

     FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, FROSTI, FSTA, BIOSIS,
     JICST-EPLUS, JAPIO' ENTERED AT 12:07:17 ON 25 APR 2002
L1             0 S FACTOR VII/VWF-COMPLEX
L2         45210 S FACTOR VIII
L3         11612 S VWF
L4          2771 S L2 AND L3
L5          4273 S CATION-EXCHANGER
L6           219 S VWF MULTIMER
L7             0 S L5 AND L4
L8           337 S L4 AND PREPARATION
L9           179 S L4 AND RECOVERY
L10            0 S L9 AND L5
L11            7 S L9 AND L6
L12      7046491 S HIGH OR LOW MULTIMER

=> s l12 and l4

L13          810 L12 AND L4

=> s l13 and l5

L14            0 L13 AND L5
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